"I'S" IN NEURO-OPTOMETRY: INFLAMMATORY THYROID ORBITOPATHY

The “I’s” in Neuro-Optometry

Iatrogenic #1: Medication Related Conditions
Iatrogenic #2: Perioperative Vision Loss
Inflammatory Thyroid Orbitopathy
Autoimmune Conditions
Abnormal Intracranial Pressures

THYROID EYE DISEASE

- Uncomfortable, potentially disabling inflammation of orbit and adnexa
- Most common autoimmune disease of the orbit
- Can occur in all thyroid conditions but majority (80%) have Graves’ hyperthyroidism
- May be the only manifestation of underlying thyroid dysfunction

PATHOPHYSIOLOGY

Orbital infiltration by B and T cells cause hyaluronidase accumulation and adipogenesis

- fat expansion: conjunctival and eyelid edema, apical compression of nerve
- levator muscle inflammation: lid retraction, proptosis, ocular exposure
- EOM expansion: diplopia

DISCLOSURES

No financial relationship with any company or product mentioned in this presentation.

OVERVIEW

- Background
- Assessment
- Psychosocial Impact
- Activity and Severity Scoring
- Current Research and Treatment Options
**RISK FACTORS**

- Smoking
- Family history of TED
- Diabetes
- Acute stress
- Prior radioactive iodine therapy

**PSYCHOSOCIAL IMPACT OF THYROID ORBITOPATHY**

- Appearance and functional difficulties due to diplopia, blur and pain are associated with significant psychological effects
- Patients with GO have higher rates of anxiety and depression compared to the national prevalence
- Patients with GO have an equivalent or poorer QOL than patients with diabetes, emphysema, or heart failure

**NATURAL COURSE**

Active phase: orbital fibroblasts drive soft tissue inflammation and EOM enlargement
- Can last up to 24 months
- Can be reactivated

**ACTIVITY AND SEVERITY SCORING**

- **Activity**
  - CAS (Clinical Activity Score)
- **Severity**
  - VISA (Vision, Inflammation, Strabismus, Appearance)
  - NOSPECS
  - EUGOGO (European Group on Graves’ Orbitopathy)
# Activity and Severity Scoring

### Activity Scoring: Clinical Activity Score (CAS)

- CAS (Clinical Activity Score)

### Severity Scoring: VISA

- Vision, Inflammation, Strabismus, Appearance

### Severity Scoring: NOSPECS

- No specific descriptors

### Activity and Severity Scoring

<table>
<thead>
<tr>
<th>Activity</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS (Clinical Activity Score)</td>
<td>VISA (Vision, Inflammation, Strabismus, Appearance)</td>
</tr>
</tbody>
</table>

**ACTIVITY SCORING: CLINICAL ACTIVITY SCORE (CAS)**

- Summed score of periocular inflammatory features
- 80% positive predictive value to predict response to corticosteroid therapy
- Cons: binary scale, equal weight for all clinical features

**SEVERITY SCORING: VISA**

- Evaluates each of the 4 categories independently
- Progression = worsening of 2+ categories

**SEVERITY SCORING: NOSPECS**

- Descriptors are loosely defined
- Difficult to assess severity of disease course due to independent grading of signs
- Does not recommend suggestions for management

---

### Activity Scoring: Clinical Activity Score (CAS)

- Initial exam: score of $\geq 3/7$ active
- Subsequent exams: score of $\geq 4/10$ active
### Severity Scoring: EUGOGO

**European Group on Graves' Orbitopathy**

- Mild, moderate to severe, and sight threatening categories
- Moderate is the broadest category including motility impairment, severe proptosis

<table>
<thead>
<tr>
<th>Severity</th>
<th>Active Treatment</th>
<th>Inactive Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Artificial tear, Selenium supplementation (100mg daily)</td>
<td>Artificial tear, Selenium supplementation (100mg daily)</td>
</tr>
<tr>
<td>Normal</td>
<td>Propranolol</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Normal</td>
<td>Local measures</td>
<td>Local measures</td>
</tr>
<tr>
<td>Mild</td>
<td>Lateral tarsorrhaphy, orbital decompression, amniotic membrane transplantation</td>
<td>Lateral tarsorrhaphy, orbital decompression, amniotic membrane transplantation</td>
</tr>
<tr>
<td>Severe</td>
<td>1. Oral methylprednisolone 1g IV methylprednisolone x 3 days, repeat after a week 2. If predominantly muscular involvement: orbital radiotherapy (not in &gt;35 years or diabetic) 3. Radiosurgery after 6 months of devonage surgery stability 4. Botulinum toxin in Muller muscle 5. Lateral tarsorrhaphy, orbital decompression 6. Propranolol 7. Local measures</td>
<td>1. Oral methylprednisolone 1g IV methylprednisolone x 3 days, repeat after a week 2. If predominantly muscular involvement: orbital radiotherapy (not in &gt;35 years or diabetic) 3. Radiosurgery after 6 months of devonage surgery stability 4. Botulinum toxin in Muller muscle 5. Lateral tarsorrhaphy, orbital decompression 6. Propranolol 7. Local measures</td>
</tr>
</tbody>
</table>

### Treatment

- Varies based on activity and severity
- Based on metaanalyses, 20% will require some form of surgery for either active or inactive GO

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Primary Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>Primary outcomes: Improvement in VA and GO-QOL questionnaire, reduction in diplopia</td>
</tr>
<tr>
<td>Placebo</td>
<td>Treatment group: significantly better outcome in all categories vs placebo with few serious adverse events</td>
</tr>
</tbody>
</table>

### Teprotumumab for the Treatment of Active Thyroid Eye Disease

- Teprotumumab (teprotumumab): IGF-IR inhibitor infusion
- Causes hyaluronan accumulation in orbital fat/muscle
- For retraction: Levator recession, lower lid retractors
- For drooping: Mullerectomy, forehead advancement
- In <35 years or diabetic

- Minimum dose: 250mg/week x 6 weeks
- Maximum dose: 500mg/week x 6 weeks
- If unresponsive: urgent orbital decompression +/- IV glucocorticoids
- If still persistent: continue up to max cumulative dose of 8g
- If unresponsive: urgent orbital decompression +/- IV glucocorticoids

### Medical Details

- **TEPEZZA** (teprotumumab): IGF-IR Inhibitor
- **IGF-IR**: expressed in fibroblasts on orbit, skin, thyroid in Graves’
- **Primary endpoint**: proptosis improvement at week 24 (reduction of ≥2mm)
- **Secondary endpoints**: improvement in VAs and GO-QOL questionnaire, reduction in diplopia
- **Treatment group**: significantly better outcome in all categories vs placebo with few serious adverse events
Teprotumumab for Thyroid Eye Disease

**TREATMENT**

All patients: Restore euthyroidism, avoid smoking, monitor activity, local measures

Severity | Active | Inactive
--- | --- | ---
Mild | • Artificial tears  
• Selenium supplementation: 100ug daily/6mo  
• Fresnel prism  
• Botulinum toxin in Muller muscle | • Artificial tears  
• Frac | Moderate- | IV methylprednisolone  
500mg/week x 6 weeks  
250mg/week x 6 weeks  
If still persistent: continue up to max cumulative dose of 8g  
If predominantly muscular involvement: orbital radiotherapy (not <35 years or diabetic)  
Teprotumumab (Tepezza) infusions (IGF-IR inhibitor) | Severe | • Orbital decompression of 2-3 walls depending on severity  
1. Strabismus surgery after 6 months of deviation angle stability  
2. Palpebral surgery  
1. For retraction: Levator recession, lower lid retractors  
2. Blepharoplasty  
1g IV methylprednisolone x 3 days, repeat after a week  
If unresponsive: urgent orbital decompression +/- radiotherapy +/- IV glucocorticoids  
Urgent deep orbital medial wall decompression  
Lateral tarsorrhaphy, orbital decompression, amniotic membrane transplant, corneal transplant  
Sight threatening: severe exposure keratopathy

**NEW THERAPIES IN RESEARCH**

- Cyclic peptides
  - Animal models demonstrate stabilization of TSH receptor binding antibodies and decreased thyroid hyperplasia/retro-orbital fibrosis
- IL-1 antagonists
  - Block orbital fibroblasts from producing GAG in vitro

- Toclizumab: monoclonal anti-IL-6 antibody
  - Fibroblasts secrete IL-6 → adipogenesis
  - Prospective, non-randomized interventional study on 18 patients with active GO resistant to intravenous steroid therapy  
  - After 4 weeks: majority had significant reduction in proptosis, improvement in extraocular motility, and resolution of diplopia
  - Needs large scale RCTs to further assess applicability

- Azathioprine: DMARD used to treat RA, SLE, Crohn's, kidney transplant rejection

  - Multicenter, double-blind, randomized, controlled trial of 126 patients with active moderate to severe TED investigating combined use of azathioprine and oral prednisolone
  - Combination therapy may reduce the risk of GO relapse after withdrawal of steroid therapy
High Serum Cholesterol Is a Novel Risk Factor for Graves’ Orbitopathy: Results of a Cross-Sectional Study

- Free fatty acids trigger the release of IL-6 and TNF-α
- Retrospective study of 126 patients with GD scheduled to undergo radioiodine treatment who discontinued statins
- CAS was significantly higher in those with high total cholesterol after adjustment for GO duration
- Cholesterol may be associated with more active forms of GO

CASE REPORT: 73 YEAR OLD WHITE MALE

73 YEAR OLD WHITE MALE

• CC: Patient says he gets double vision all the time that resolves when looks down. Diplopia is vertical and binocular, constant low level since last summer.
• Medical history: Hyperthyroidism, sleep apnea, colon polyps, seborrheic keratosis, hypertension, epidermal cyst
• Medication: Vitamin D3, lisinopril, omeprazole, aspirin
• (-) Smoker

73 YEAR OLD WHITE MALE

• Best corrected acuities: OD 20/30-2 OS 20/25-2
• Pupils, confrontation fields, and color vision normal with CN III-VII intact
• Hertel exophthalmometry: 15<116>20mm

73 YEAR OLD WHITE MALE

Cover Test:  Noncomitant LET and LHT

<table>
<thead>
<tr>
<th>Cover Test</th>
<th>OD ductions</th>
<th>OS ductions</th>
</tr>
</thead>
<tbody>
<tr>
<td>OD ductions</td>
<td>-2</td>
<td>-2</td>
</tr>
<tr>
<td>OS ductions</td>
<td>-2</td>
<td>0</td>
</tr>
</tbody>
</table>

73 YEAR OLD WHITE MALE

<table>
<thead>
<tr>
<th>Test</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lid</td>
<td>periorbital fat prolapse under LL, mild lid edema</td>
<td>periorbital fat prolapse under LL, mild lid edema</td>
</tr>
<tr>
<td>Cornea</td>
<td>no significant PEE</td>
<td>no significant PEE</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>2+ Conjunctival injection, 2+chemosis; No conjunctival papillae or follicles</td>
<td>2+ Conjunctival injection, 2+chemosis; No conjunctival papillae or follicles</td>
</tr>
<tr>
<td>Ant. Chamber</td>
<td>Deep &amp; Quiet</td>
<td>Deep &amp; Quiet</td>
</tr>
<tr>
<td>I’s</td>
<td>Normal, (-)INX</td>
<td>Normal, (-)INX</td>
</tr>
<tr>
<td>Tonometry @ 10/15min with GAT</td>
<td>28mmHg</td>
<td>32mmHg</td>
</tr>
</tbody>
</table>
**73 YEAR OLD WHITE MALE**

<table>
<thead>
<tr>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lens</td>
<td>Clear PC IOL</td>
</tr>
<tr>
<td>Verrous</td>
<td>clear</td>
</tr>
<tr>
<td>Optic disc</td>
<td>Temporal pallor, no edema, no disc heme, Small nerve.</td>
</tr>
<tr>
<td>Macula</td>
<td>No heme, exudate, or edema</td>
</tr>
<tr>
<td>Vessels</td>
<td>Normal</td>
</tr>
<tr>
<td>Posterior Pola</td>
<td>Normal</td>
</tr>
<tr>
<td>Periphery</td>
<td>No retinal holes, tears or detachment</td>
</tr>
</tbody>
</table>

**MRI HEAD/Brain AND/OR BRAIN STEM WITH CONTRAST**

- Enlarged medial and inferior and possibly to lesser extent superior rectus muscles bilaterally, suspicious for thyroid orbitopathy.

**FREE T4**  >7.8ng/dL  TSH  0.01 L  TSH  0.7 - 1.7

- CAS score was 4/7: active moderate-severe GO
- Started on 12 weeks of IV steroids for strabismus and anterior thyroid eye disease findings, concern for early compressive optic neuropathy
- Start latanoprost OU qhs for IOP control
73 YEAR OLD WHITE MALE

3/2015: choroidal folds and DON, MRI confirms EOM swelling
9/2015: IV steroid treatment, stable compressive optic neuropathy
7/2017: strabismus surgery with resolution of diplopia in primary gaze
12/2017: s/p thyroidectomy, monitored by endocrinology without treatment

77 YEAR OLD WHITE MALE

CC: Denies ocular pain, diplopia in primary gaze. Patient reports that vision is doing good.
No changes in medical history or medications
Best corrected acuities: OD 20/20-1 OS 20/20
Pupils, confrontation fields, and color vision normal
Anterior and posterior segment unremarkable for signs of thyroid eye disease

77 YEAR OLD WHITE MALE

Cover Test: Ortho in primary gaze with LET and LHT in left upgaze only

OD: ductions
-2  -2  -2  -1  -1  -1
0    0    0    0    0

OS: ductions
0    0    0    0    0    0
SUMMARY

- GO is the most common autoimmune disease of the orbit
- Patients can suffer from significant psychosocial effects
- Assessing activity and severity are crucial for appropriate management and treatment
- Tepezza (teprotumumab) is the first FDA approved treatment for active GO and can improve proptosis and diplopia

REFERENCES


QUESTIONS AND COMMENTS

Allison Kuo, OD
Primary Care & Ocular Disease Resident
VA Portland Health Care System
allison_kuo@berkeley.edu
The “I’s” in Neuro-Optometry:
Autoimmune Diseases

Felix Wong, OD
Primary Care & Ocular Disease Resident
VA Portland Health Care System
June 4th, 2021
Northwest Residents Conference

Iatrogenic #1: Medication Related Conditions
Iatrogenic #2: Perioperative Vision Loss
Inflammatory Thyroid Orbitopathy
Autoimmune Conditions
Abnormal Intracranial Pressures

DISCLOSURES
I have no financial relationship with any company or products mentioned in this presentation

The “I’s” in Neuro-Optometry

58-YEAR-OLD FEMALE

- CC: Bilateral ocular/periorbital pain localized to forehead and temples x 1.5 weeks prior with more recent exacerbations
- Improvement in dark room or when closing eyes
- Family history of glaucoma (grandmother)
- Hyperlipidemia, bipolar disorder, sleep apnea

EXAM FINDINGS

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>20/50, PH: 20/30, PAP: 20/25</td>
<td>20/40, PH: 20/30, PAP: 20/25</td>
</tr>
<tr>
<td>Pupils</td>
<td>Equal, round, reactive to light OU, (-)APD</td>
<td></td>
</tr>
<tr>
<td>EOM</td>
<td>Full &amp; Comitant OU</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain in Peripheral Gaze (Worst in Up and Right Gaze)</td>
<td></td>
</tr>
<tr>
<td>Confrontation VF</td>
<td>FTFC</td>
<td>FTFC</td>
</tr>
<tr>
<td>Tonometry</td>
<td>12 mmHg</td>
<td>12 mmHg</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>0.10 c/d. (-)Disc edema/pallor</td>
<td>0.10 c/d. (-)Disc edema/pallor</td>
</tr>
</tbody>
</table>
**NEURO-OPHTHALMOLOGY E-CONSULT**

- Concern for acute optic neuritis or bilateral optic neuropathy
- Recommended MRI w/wo contrast within the next two weeks
- F/u in neuro-ophthalmology in 1 week

**ED VISIT (ON-CALL OPHTHALMOLOGY)**

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>HM 1’</td>
<td>CF 1’</td>
</tr>
<tr>
<td>Pupils</td>
<td>Equal, round, reactive to light OU, 2+ Right APD</td>
<td></td>
</tr>
<tr>
<td>EOM</td>
<td>Full &amp; Comitant OU Pain in Peripheral Gaze (Worst in Up and Right Gaze)</td>
<td></td>
</tr>
<tr>
<td>Tonometry</td>
<td>16 mmHg</td>
<td>16 mmHg</td>
</tr>
<tr>
<td>Optic disc</td>
<td>0.10 c/d, (-)Disc edema/pallor</td>
<td>0.10 c/d, (-)Disc edema/pallor</td>
</tr>
</tbody>
</table>

**NEXT DAY WITH NEURO-OPHTHALMOLOGY**

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>HM 1’</td>
<td>HM 3’</td>
</tr>
<tr>
<td>Pupils</td>
<td>Equal, round, reactive to light OU, 2+ Right APD</td>
<td></td>
</tr>
<tr>
<td>EOM</td>
<td>Full &amp; Comitant OU Pain in Peripheral Gaze (Worst in Up and Right Gaze)</td>
<td></td>
</tr>
<tr>
<td>Confrontation VF</td>
<td>Constricted 360° except infero inferior midperiphery</td>
<td>Constricted 360° except supero superior midperiphery</td>
</tr>
<tr>
<td>Color vision</td>
<td>Unable to see test plates</td>
<td>Unable to see test plates</td>
</tr>
<tr>
<td>Tonometry</td>
<td>12mmHg</td>
<td>12mmHg</td>
</tr>
<tr>
<td>Optic disc</td>
<td>0.10 c/d, Subtle Elevation</td>
<td>0.10 c/d, Subtle Elevation</td>
</tr>
</tbody>
</table>
**ASSESSMENT/PLAN**

- **Assessment:**
  - Bilateral Retrobulbar Optic Neuritis
  - Non-organic vision loss
- **Treatment**
  - Begin IV Methylprednisolone (IVMP) 1000mg q24hrs for 5 days
  - Consider IV Immunoglobulin (IVIG)/Plasma Exchange (PLEX) if no response to steroids

**BILATERAL OPTIC NEURITIS**

- **Studies Ordered by Ophthalmology:**
  - Rule out Syphilis (FTA-Abs, RPR), Sarcoidosis (CT chest, ACE), ANCA, ANA
  - LP w/ opening pressure, CBC with Diff, Cytology, HSV, Oligoclonal Bands/MS Panel, NMO IgG/Aquaporin-4 Ab, Anti-mog Ab

**DISEASE TYPES**

- Relapsing-remitting (85-90%)
  - Age: 30 years old
  - 3x more common in females
  - Primary progressive (10-15%)
  - Age: 40 years old
  - Males=Females

**CLINICAL PRESENTATION OF MS**

- **Pathophysiology:**
  - Oligodendrocyte and myelin loss shown to be accompanied by inflammatory mediators
  - Inflammation causes edema within the myelinated nerve sheaths
- **Typical Presentation:**
  - Acute, unilateral optic neuritis
  - Double vision (<40 years old)
  - Facial sensory loss or trigeminal neuralgia (<40 years old)
  - Partial myelopathy
  - Asymmetric limb weakness
  - Urge incontinence or erectile dysfunction
Optic nerve sequelae:
- Retrobulbar optic neuritis
- Papillitis
- Peri-neuritis
- Neuro-retinitis

Oculomotor sequelae:
- Internuclear ophthalmoplegia
- Nystagmus
- Skew deviation
- Cranial nerve palsies

Multiple sclerosis-associated uveitis:
- Bilateral intermediate uveitis or panuveitis

TREATMENT OF MS
- ONTT Study: 1g IV methylprednisolone for 3 days followed by oral steroid taper
- No neurologic benefit to oral prednisone taper
- Bioequivalent doses (1250 mg) of ORAL corticosteroids may be used as alternative to IV corticosteroids

OVERVIEW OF NMOSD
Epidemiology
- 9x more prevalent in women than men
- Median age of onset is 39
No pathognomonic clinical characteristic:
- Relapsing-remitting (90%)
- Bilateral or rapidly sequential optic neuritis
- Longitudinally extensive transverse myelitis AND optic neuritis
- More severe disease course with higher relapse rate often without complete recovery

Neuromyelitis Optica Spectrum Disorder (NMOSD)
- Traditional Neuromyelitis Optica (NMO)
- AQP4-IgG seropositive with limited forms of NMO
- Cerebral, diacritic, and bracten lesions that occur in patients with NMO
- AQP4-IgG seropositive with coexisting autoimmune disorders (Lupus, Sjogren’s, or Myasthenia Gravis)
- Opticospinal form of MS (Prominent MS phenotype in Asia)
**PATHOPHYSIOLOGY OF NMOSD**

- Autoimmune, inflammatory by NMO-IgG (anti-AQP4)
- Antibodies recruit inflammatory mediators with eventual loss of oligodendrocytes or neurons
- Necrosis of both gray and white matter
- Heterogeneity due to wide distribution of AQP4 within brain parenchyma
- Predilection for optic nerve and spinal cord

**TESTING FOR NMOSD**

<table>
<thead>
<tr>
<th>Serologic Testing</th>
<th>CSF Testing</th>
<th>MRI</th>
<th>Coexisting Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• AQP4-IgG</td>
<td>• Absence of oligoclonal bands</td>
<td>• Longitudinally Extensive Transverse Myelitis (LETM)</td>
<td>• SLE, Sjogren’s Syndrome, Myasthenia gravis</td>
</tr>
</tbody>
</table>

**TREATMENT AND PROGNOSIS OF NMOSD**

- Chronic immunotherapy
- Monoclonal antibodies
- Soliris (eculizumab): Complement protein C5
- Upliva (inhibinab-cdon): CD19
- Emspryng (natalizumab-mwge): IL-6
- Azathioprine, prednisone, methotrexate, cyclosporine, tacrolimus
- Resolution often incomplete and likelihood of relapse higher than MS

**Optic neuritis**

- Unilateral
- Bivascular
- Bivascular

**Sex**

- Female
- AQP4(+), Female
- AQP4(-), Male/Female
- Female slightly more than male

**Type**

- Relapsing or progressive
- Relapsing
- Monophasic or relapsing

**Sero/CSF testing**

- Oligoclonal bands in CSF
- NMO/AQP4 Antibodies
- MOG Antibodies

**MRI findings**

- Multifocal lesions within optic nerve, spinal cord, or brain
- Longitudinally extensive myelitis and optic neuritis
- Longitudinally extensive myelitis or optic neuritis

**Visual Recovery**

- Often full recovery
- Incomplete recovery
- Often full recovery

**Multiple Sclerosis (MS)**

<table>
<thead>
<tr>
<th>Neurromyelitis Optica Spectrum Disorder (NMOSD)</th>
<th>Myelin Oligodendrocyte Glycoprotein (MOG)-Antibody Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic neuritis</td>
<td>Bivascular</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Type</td>
<td>Relapsing or progressive</td>
</tr>
<tr>
<td>Sero/CSF testing</td>
<td>Oligoclonal bands in CSF</td>
</tr>
<tr>
<td>MRI findings</td>
<td>Multifocal lesions within optic nerve, spinal cord, or</td>
</tr>
<tr>
<td>Visual Recovery</td>
<td>brain</td>
</tr>
</tbody>
</table>

**TREATMENT**

- Chronic immunotherapy
- Monoclonal antibodies
- Soliris (eculizumab): Complement protein C5
- Upliva (inhibinab-cdon): CD19
- Emspryng (natalizumab-mwge): IL-6
- Azathioprine, prednisone, methotrexate, cyclosporine, tacrolimus
- Resolution often incomplete and likelihood of relapse higher than MS

**PROGNOSIS**

- Chronic immunotherapy
- Monoclonal antibodies
- Soliris (eculizumab): Complement protein C5
- Upliva (inhibinab-cdon): CD19
- Emspryng (natalizumab-mwge): IL-6
- Azathioprine, prednisone, methotrexate, cyclosporine, tacrolimus
- Resolution often incomplete and likelihood of relapse higher than MS
BACKGROUND OF MOG

- Myelin oligodendrocyte glycoprotein is one of many different glycoproteins within myelin of the CNS, located on surface of myelin sheaths and oligodendrocytes
- Epidemiology
  - Female slightly more common than male
  - Younger

Epidemiology

Neuromyelitis Optica Spectrum Disorders (NMOSD)

AQP4 Seropositive
MOG Seropositive
Negative Serology

CLINICAL CHARACTERISTICS OF MOG

- Optic neuritis (54-61%), often bilateral
- Compared to NMOSD, transverse myelitis less common
- Predilection for optic nerve and spinal cord involvement, often isolated
- Monophasic in up to 50% of cases
- Tend to have better long-term visual acuity outcomes compared to NMOSD
- In children, phenotypic presentation similar to Acute disseminated encephalomyelitis (ADEM)

DIAGNOSIS OF MOG

MRI
- Optic nerve
- Usually posterior but tends to be more anterior than NMOSD
- Spinal cord
- Brain
- Normal in 2/3 of cases

Serologic Testing
- MOG IgG

TREATMENT AND PROGNOSIS OF MOG

- Treatment
- Lack of studies and guidelines regarding treatment
- Current research involves chronic immunotherapy, immunosuppressive agents seen in AQP4 NMO, or other MS therapies
- Lower risk for relapses and have better visual and motor outcomes compared with NMOSD
58-YEAR-OLD FEMALE

- IV Methylprednisolone (IVMP) 1g for 5 days, followed by 5 days of Plasma Exchange (PLEX) by neurology

>1 YEAR LATER

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>20/25</td>
<td>20/25</td>
</tr>
<tr>
<td>Pupils</td>
<td>Equal, round, reactive to light OU, (-)RAPD</td>
<td></td>
</tr>
<tr>
<td>EOM</td>
<td>Full &amp; Comitant OU</td>
<td></td>
</tr>
<tr>
<td>Confrontation VF</td>
<td>FTFC</td>
<td>FTFC</td>
</tr>
<tr>
<td>Color vision</td>
<td>10/20 HRR (questionable)</td>
<td>19/20 HRR</td>
</tr>
<tr>
<td>Optic Disc</td>
<td>0.10 c/d, Mild Pallor, no edema</td>
<td>0.10 c/d, Mild Pallor, no edema</td>
</tr>
</tbody>
</table>
These patients may have permanently impaired contrast sensitivity or color vision, even with full acuity recovery.

Clinical outcome of NMOSD tends to be more severe.

Demyelinating conditions:
- Multiple Sclerosis is the most common and classic demyelinating disease
- Neuromyelitis Optics Spectrum Disorder (AQP4 antibodies)
- Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOG antibodies)
- SUSPECT NMOSD or MOG in cases of bilateral optic neuritis

Thank you!

**REFERENCES**


**QUESTIONS?**

Felix.Wong@va.gov